

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board:

Paper No. 22

**UNITED STATES PATENT AND TRADEMARK OFFICE**

**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Ex parte LYLE ARNOLD, TOD BEDILION,  
ERIK BJELDANES, THOMAS THERIAULT and WARREN LEI

Appeal No. 2003-0335  
Application No. 09/586,156

ON BRIEF

**MAILED**

**FEB 26 2004**

U.S. PATENT AND TRADEMARK OFFICE  
BOARD OF PATENT APPEALS  
AND INTERFERENCES

Before ADAMS, MILLS and GREEN, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

**DECISION ON APPEAL**

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 1, 2, 3, 8-13 and 15-23, which are all of the claims pending in this application.

Claims 1 is illustrative of the claims on appeal and reads as set forth below:

1. A method for immobilizing a polynucleotide probe comprising the steps of: combining the probe with a polynucleotide target stably associated with a surface of a solid support, wherein one of the probe and the target is double-stranded comprising complementary strands, and the other is single-stranded having complementarity with one of the complementary strands, under conditions wherein the probe and target hybridize and the probe is thereby immobilized.

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The references are relied upon by the examiner are:

Brown et al. (Brown)                      5,807,522                      Sept. 15, 1998

Pease et al. (Pease), "Light-generated oligonucleotide arrays for rapid DNA sequence analysis," Proc. Nat. Acad. Sci., Vol. 91, pp. 5022-5026 (1994)

Tygai et al. (Tygai), "Molecular Beacons: Probes that Fluoresce upon Hybridization," Nature Biology, Vol. 14, pp. 303-308 (1996)

Rickwood, D., ed. (Anderson), Nucleic Acid Hybridization: A Practical Approach, IRL Press, Ltd., Oxford, England, pp. 86-109 (1985).

Bates et al. (Bates), "Detection and kinetic studies of triplex formation by oligodeoxynucleotides using real-time biomolecular interaction analysis (BIA)," Nucleic Acids Research, Vol. 23, No. 18, pp. 3627-3632 (1995)

#### Grounds of Rejection

Claims 1, 2, 8, 11, 15, 16, 22 and 23 stand rejected under 35 U.S.C. § 102(b) as anticipated by Bates.

Claims 1, 2, 8-13 and 15-23 stand rejected under 35 U.S.C. § 103(a) as obvious over Tyagi in view of Pease.

Claims 3 stands rejected under 35 U.S.C. § 103(a) as obvious over Tyagi in view of Pease and Anderson.

Claims 14 and 24 stand rejected under 35 U.S.C. § 103(a) as obvious over Tyagi in view of Pease and Brown.

We reverse the rejections under 35 U.S.C. § 103(a) and affirm the rejection of the claims under 35 U.S.C. § 102(b) over Bates.

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### Claim Grouping

According to appellants, the claims stand or fall together in the following groups: Group 1, claims 1, 2, 8, 11, 15, 16, 22 and 23; Group 2, claims 1, 2, 8-13; Group 3, claims 15-23; Group 4, claim 3, and Group 5, claim 14; Group 6, claim 24. (Brief, page 3). Since the separate claim groupings and individual claims of each group are not argued, we decide this appeal with respect to the separate prior art rejections on the basis of representative claim 1. 37 CFR §1.192(c)(7) (1996).

### DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied references, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejections, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief for the appellants' arguments thereagainst. As a consequence of our review, we make the determinations which follow.

### Claim Interpretation

Our appellate reviewing court stated in Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1567-1568, 1 USPQ2d 1593, 1597 (Fed. Cir.), cert denied, 481 U.S.

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1052 (1987):

Analysis begins with a key legal question -- what is the invention claimed? Courts are required to view the claimed invention as a whole. 35 U.S.C. 103. Claim interpretation, in light of the specification, claim language, other claims and prosecution history, is a matter of law and will normally control the remainder of the decisional process. [Footnote omitted.]

To that end, we also note that during ex parte prosecution, claims are to be given their broadest reasonable interpretation consistent with the description of the invention in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

We interpret the terms "complementary" and "complementarity" in the claims broadly and consistent with the definition set forth in the specification. The specification, page 5 states

[t]he term "complementary" or "complementarity", as used herein, refers to the natural binding of polynucleotides under permissive salt and temperature conditions by base-pairing. For example, the sequence "A-G-T" binds to the complementary sequence "T-C-A". Complementarity between two single-stranded molecules may be "partial", in which only some of the nucleic acids bind, or it may be complete when total complementarity exists between single stranded molecules. The degree of complementarity between nucleic acid strands has significant effects on the efficiency and strength of hybridization between nucleic acid strands. Thus, the element and its probe, and the contact area between the element and the probe can be described as complementary.

For reasons discussed herein, we find nothing in the definition in the specification excludes Hoogsteen complementary DNA binding.

35 U.S.C. § 102(b)

Claims 1, 2, 8, 11, 15, 16, 22 and 23 stand rejected under 35 U.S.C. § 102(b) as anticipated by Bates.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "It is also an elementary principle of patent law that when, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if one of them is in the prior art." Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 782, 227 USPQ 773, 779 (Fed. Cir. 1985).

According to the examiner, Bates teach the

detection and kinetic studies of triplex formation by oligodeoxynucleotides using real-time biomolecular interaction analysis (BIA). In this study, 5'-Biotinylated oligonucleotides were immobilized on the streptavidin-coated surface of a biosensor chip (page 3628, right column, first and second paragraphs). A single-stranded oligonucleotide (claim 22) immobilized on the chip surface was able to capture a DNA duplex by triplex recognition as described in claims 1 and 15. For example, Bt-T30 immobilized on the chip surface has been shown to capture of T30-A30 duplex...

Answer, page 4.

Bates, page 3629, column 1, also describes the "[k]inetic analysis of triplex formation by HD3." "Samples ... of HD3 were injected over immobilised Bt-HD1-HD2 duplex." Figure 2 (page 3628) shows Bt-HD1 and HD2 are antiparallel nucleotide sequences which are complementary to one another and linked by Watson-Crick type

of hydrogen pairing. HD3 is added and forms a triplex with HD1 and HD2. See also page 3631, Figure 6. According to Figure 2 of Bates, HD3 is depicted as having complementarity with one of the complementary strands, e.g. the Bt-HD1 strand. Thus, even though the HD3 may Hoogsteen bind to the Bt-HD1-HD2 immobilized duplex, it meets the claim limitation "having complementarity with one of the complementary strands."

In our view, for the reasons set forth above, the examiner has set forth a prima facie case of anticipation. After the PTO establishes a prima facie case of anticipation based on inherency, the burden shifts to the appellants to prove that the subject matter shown to be in the prior art does not possess the characteristics of the claimed invention. See In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985); In re King, 801 F.2d 1324, 1327, 231 USPQ 136, 138 (Fed. Cir. 1986).

The appellants respond to the examiner's rejection, arguing, the three triplex-forming systems of Bates are shown in Table 1. Reply Brief, page 5. Specifically,

Figure 2 [of Bates] describes each of these molecules: in each case, you have the third single stranded molecule binding the backside of the purines of the immobilized double stranded molecule. Note that the third strands are always pyrimidine polymers... There is no complementarity, as expressly required by our claims. Note that even with Bates' polyT/polyA homopolymers, the orientation of the polyT probe binding is parallel (not complementary) with the polyA of the duplex (see Fig. 2) and the polyA probe binding of the A30-A30-T30 triplex (p.3630) is antiparallel with the poly A - not with the polyT. Bates' solid phase Hoogsteen binding assay provides a useful system for studying the kinetics of this phenomenon, however it is inapplicable to other than pyrimidine probes and purine rich targets, and it is not a hybridization assay as claimed.

Reply Brief, page 5.

To support their argument, appellants argue that the term “[c]omplementary is a term of art, referring to antiparallel sequences which hybridize by Watson-Crick base pairing to form the classic double helix structure...” Reply Brief, page 2.<sup>1</sup> However, appellants have also argued in the record (Brief, page 4, footnote 1), “[w]e believe the complementarity limitation of our claim is unconditional.”

The examiner responds to appellants' argument, stating that (Answer, page 6)

at least two types of hydrogen pairings exist in nucleic acid double helix, Watson-Crick type of hydrogen pairing and non-Watson-Crick interaction, known as Hoogsteen pairing... Since “complementary” or “complementarity” in the specification is defined as “the natural binding of polynucleotides under permissive salt and temperature conditions by base pair” (see page 5, second paragraph), it is clear that appellant’s definition of complementarity does not limit “complementarity” to Watson-Crick type of hydrogen pairing. Hoogsteen pairing between pyrimidine and purine can also be considered as complementary. Second, from the definition of “complementarity” in the specification ..., it is clear that appellant’s definition of complementarity does not limit to the orientation wherein the polyT probe binding is anti-parallel with the polyA of the duplex since there is no word “parallel” or “anti-parallel” in the definition. Third, since Bates *et al.*, did not teach a A30-A30-T30 triplex but taught a A30-T-30-A30 triplex ... appellant’s interpretation to the reference of Bates *et al.*, is incorrect.

We agree with the examiner that the terms “complementary” and “complementarity” as defined in the specification, do not exclude an alternative, natural structure of

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<sup>1</sup>Appellants also proffer textual material describing Hoogsteen binding and the formation of the DNA double helix, not previously of record. Reply Brief, pages 2-3. We do not find that this supplementary material alters the definitions of the terms “complementary” and “complementarity” set forth in the specification.

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DNA, including Hoogsteen binding.<sup>2</sup> Therefore, we agree with the examiner that the triplex structures shown in Bates and their use in an assay, anticipate the claimed method. In view of the above, we affirm the rejection of claims over Bates.

35 U.S.C. § 103(a)

Claims 1, 2, 8-13 and 15-23 stand rejected under 35 U.S.C. § 103(a) as obvious over Tyagi in view of Pease. Claims 3 stands rejected under 35 U.S.C. § 103(a) as obvious over Tyagi in view of Pease and Anderson. Claims 14 and 24 stand rejected under 35 U.S.C. § 103(a) as obvious over Tyagi in view of Pease and Brown.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). It is well-established that the conclusion that the claimed subject matter is prima facie obvious must be supported by evidence, as shown by some objective teaching in the prior art or by knowledge generally available to one of ordinary skill in the art that would have led that individual to combine the relevant teachings of the references to arrive at the claimed invention. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

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<sup>2</sup> Hoogsteen binding also involves complementary base pairing. Note, page 40 of Molecular Biology and Biotechnology, Ed. Robert A. Myers, 1995, attached to the Reply Brief, indicates oligonucleotide analogues "should be able to form stable Watson-Crick or Hoogsteen complexes with complementary target sequences under physiological conditions." Here Hoogsteen binding to the target sequence is indicated to be "complementary". [Emphasis added.]



According to the examiner, Tyagi teach probes which “comprise covalently linked and non-covalently linked complementary strands with a hairpin structure” and which undergo a spontaneous fluorogenic conformation change when they hybridize to their targets. Answer, page 8. The examiner acknowledges that Tyagi does not disclose a support with an immobilized oligonucleotide. Id. The examiner relies on Pease for the disclosure of a microarray of immobilized targets. Id.

In response, appellants point out that, in Tyagi, the complementary arm sequences are “unrelated to the target sequence”. Reply Brief, page 6. According to appellants, for this reason “Tyagi can not meet or suggest (and necessarily teaches directly away from) our method's requirement that the single stranded component (here, the target) have complementarity with one of the strands of the double-stranded component (here, the probe).” Id.

Upon review of Tyagi, we agree with appellants that the hairpin molecular beacon probe structure disclosed therein does not meet the claim requirement that “one of the probe and the target is double-stranded comprising complementary strands, and the other is single-stranded having complementarity with one of the complementary strands”. [Emphasis added.]

The probe of Tyagi is the basis of each of the obviousness rejections before us. We agree with appellants that the probe of Tyagi does not meet the requirements of the probe used in the claimed method. We do not find that the secondary references cited overcome the deficiencies of the probe of Tyagi and its failure to meet the claim

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requirements.

The rejections of the claims for obviousness are reversed.


CONCLUSION

We reverse the rejections under 35 U.S.C. § 103(a) and affirm the rejection of the claims under 35 U.S.C. § 102(b) over Bates.

AFFIRMED-IN-PART

  
DONALD E. ADAMS  
Administrative Patent Judge

  
DEMETRA J. MILLS  
Administrative Patent Judge

  
LORA M. GREEN  
Administrative Patent Judge

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